

## Indian Academy of Pediatrics (IAP)



# nRICH

**N**ewer **R**esearch and recommendations **I**n **C**hild **H**ealth

Lead Author  
*Prakash Vaidya*

Co-Author  
*Indu Khosla*



## UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

**Uendra Kinjawadekar**

IAP President 2023

**GV Basavaraja**  
IAP President 2024

**Remesh Kumar R**  
IAP President 2022

**Vineet Saxena**  
IAP HSG 2022-23

**Dear fellow IAPans,**

**nRICH**

**Newer Research and recommendations In Child Health**-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialties of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology, vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

*Upendra Kinjawadekar*  
*National President 2023*  
*Indian Academy of Pediatrics*



© Indian Academy of Pediatrics

## **Chairperson**

Upendra Kinjawadekar

## **Convenor**

Vijay Yewale

## **IAP nRICH team**

Arun Bansal

Vaman Khadilkar

Indu Khosla

Srinivas Murki

Nitin K Shah

Tanu Singhal

Rhishikesh Thakre

Prakash Vaidya

SK Yachha

# The Effects of Increasing Fruit and Vegetable Intake in Children with Asthma on the Modulation of Innate Immune Responses.

Prakash Vaidya<sup>1</sup>, Indu Khosla<sup>2</sup>

Consultant Pulmonologist and Sleep Expert, NH SRCC Hospital for children Nanavati Max superspecialty Hospital Lilavati Hospital and Research Centre, Mumbai, India <sup>1</sup>,  
Consultant Pediatrician, Fortis Hospital, Mumbai, India <sup>2</sup>

## BASED ON ARTICLE

Banafsheh Hosseini, Bronwyn S. Berthon , Megan E. Jensen , Rebecca F. McLoughlin, Peter A. B. Wark, Kristy Nichol, Evan J. Williams , Katherine J. Baines , Adam Collison , Malcolm R. Starkey , Joerg Mattes and Lisa G. Wood. *Nutrients*. 2022;14:3087.

## Summary

**Background:** Asthma is the most prevalent chronic childhood disease and children with asthma often have flare-ups. Asthma flareups cause ER visits, admissions, and even mortality. Rhino viruses (RV1B) are the commonest cause of exacerbations, as are also House Dust Mite (HDM) exposure and high levels of household Lipopolysaccharide (LPS). Toxicologic and epidemiologic studies have demonstrated that environmental endotoxins like LPS cause inflammatory and atopic responses in both non-asthmatic and asthmatic subjects. Inhaled Corticosteroids ICS are the standard treatment, for Asthma control but they are far from perfect. Is there any possible non-pharmacological intervention to reduce/prevent flare ups? In this context, many epidemiological studies have shown that fruit and vegetable intake (F&V) is associated with decrease in the risk of wheezing (including asthma) and it also positively impacts lung function. A previous study by the same authors conducted in 137 adult patients with asthma, had reported that those assigned to a low versus a high F&V diet for 14 weeks had a 2.26-fold increased risk of an asthma exacerbation. This prompted the present study for the paediatric population.

**Method:** This study was conducted in a hospital in Australia. Inclusion criteria were: Children aged 3–11 years with a physician diagnosis of Asthma; recent exacerbation/s ( $\geq 1$  exacerbation in the preceding 6 months or  $\geq 2$  in the past 12 months); or those with stable Asthma at the initial clinic visit (defined as no change in Asthma medications, unscheduled medical visit for asthma, use of OCS or antibiotics in preceding 4 weeks); consuming  $\leq 3$  serves of F&V per day (assessed over the past week); willingness and ability to attend clinic appointments; desire to comply with proposed dietary changes; and agreement to collect blood samples for research purposes at clinic visits.

Exclusion criteria included other respiratory conditions, diagnosed intestinal disorders, or consumption of nutritional supplements (in the previous 4 weeks).

These children were randomly assigned to a high F&V diet or control (usual diet) for 6 months. The participants in the control group, blinded to the study hypothesis, continued their usual diet ( $\leq 3$  serves/d F&V).

During episodes of exacerbation or URTI, parents were asked to fill a questionnaire, and collect a nasal swab.

High-Performance Liquid Chromatography (HPLC) was used to measure plasma carotenoid concentrations (as a measure of F&V consumption). Cell culture supernatant concentrations of IFN- $\gamma$ , IL-1 $\beta$  and IL-6, were analysed using a bead-based multiplex assay

These levels were done at baseline, 3 months and 6 months.

**Outcome:** This study looked at (1) frequency of respiratory-related adverse events, (2) severity and duration of Asthma Exacerbations, (3) viral detection in nasal swabs collected during asthma-related events, and (4) in-vitro cytokine production in PBMCs (Peripheral Blood Mononuclear Cells) treated with different stimuli.

#### Changes in Fruit and Vegetable Intake and Plasma Carotenoids

F&V consumption over the trial duration was significantly higher in the intervention group than in the control group ( $p < 0.001$ ), and correspondingly there was a significant change in plasma carotenoid levels (as an objective biomarker of F&V intake) in this group measured at 0,3,6 months.

#### Frequency and Severity of Asthma-Related Events and Virus detection.

Three sets of events were monitored: Parent-reported asthma-related illness was categorised into three groups: (1) asthma exacerbation alone without the presence of upper respiratory tract infection (URTI) symptoms; (2) URTI alone (runny/congested nose, sore throat, earache, sneezing, with or without fever), with no asthma exacerbation; and (3) exacerbation with URTI: a parent-reported increase in cough, wheeze or shortness of breath with suspected URTI.

The distribution of reported exacerbations, URTI, and exacerbations with URTI was similar between the two groups ( $p > 0.05$ ).

**However, the high F&V diet group had significantly fewer subjects with 2 or more asthma exacerbations with URTI during the 6-month intervention (88.0% versus 63.6%,  $p = 0.049$ ).**

There was no significant difference in virus detection in this study, with a virus detection rate of just 35.6% in the intervention group and 37.5% in control subjects.

#### In Vitro PBMC (Peripheral Blood Mononuclear Cells) Cytokine Production.

**LPS-induced IFN- $\gamma$  and IFN- $\lambda$  production was significantly increased in the intervention group after 3 months, compared to baseline** whereas no significant difference had been observed at baseline.

However, at the end of the 6-month trial, no significant increase was observed in cytokine production from PBMCs stimulated with RV1B and HDM.

Correlation analysis of PBMC cytokine responses to RV1B, HDM, and LPS stimulation and plasma carotenoid levels further showed that increases in total and individual carotenoids (such as lycopene, lutein,  $\alpha$ - and  $\beta$ -carotene) were associated with higher IFN- $\lambda$  production, while low levels of these were associated with higher IL-6 and IL-1 $\beta$  production.

### **Conclusions:**

In summary, increasing F&V intake decreased asthma-related illness. This study establishes the relevance of a dietary intervention strategy—increased F&V intake—for improving innate immune responses and reducing exacerbation rates in children with asthma.

### **Commentary**

Asthma is a heterogeneous disease characterized by chronic airway inflammation which is caused by the body's innate immunological response to triggers.

The innate immune system is the first responder of host defense and comprises of cells like neutrophils, macrophages, dendritic cells, and natural killer cells. These immune regulatory cells produce proallergic, proinflammatory cytokines (IL-4, IL-5 and IL-13) and chemokines (eotaxins).

On the other hand the interferons (IFN's) are a group of cytokines that play a central role in the protection against infections and exacerbation of asthma. Type I and III IFNs (IFN $\lambda$ 1/2/3, IL-28/29) in particular play an indispensable role in the host immune system to fight off pathogens. Paediatric and adult asthmatics often have impaired IFN production. This makes them more susceptible to infection and uncontrolled Th 2 responses resulting in airway hyperresponsiveness, inflammation and asthma exacerbations.

Asthma and obesity (associated with junk food intake) are both characterized by chronic tissue inflammation mediated by the TH-2 pathway. Adipocytes release inflammatory substances including interleukin (IL-1, IL-6, and tumour necrosis factor (TNF)). The obese state, is thus associated with worse asthma severity and control, and abnormal lung function. It is well known that viral-induced exacerbations can occur despite ICS treatment in children with asthma. Dietary antioxidants can scavenge reactive oxygen species (ROS), which are increased in the airways of patients with asthma, and thus, inhibit nuclear factor-kappa B (NF $\kappa$ B)-mediated inflammation. Fruit and vegetables are high in antioxidants and anti-inflammatory phytochemicals, including carotenoids (e.g., lutein, lycopene,  $\beta$ -cryptoxanthin,  $\alpha$ -carotene and  $\beta$ -carotene) and other biologically active substances. This may improve innate immune responses in children with asthma and improve control and reduce risk of exacerbations. Hence numerous studies have investigated nonpharmacological interventions to control and manage asthma. The European Academy of Allergy and Clinical Immunology (EAACI) has also reported that increasing the dietary intake of fruit and vegetables decreases asthma incidence, particularly in children.

This study also highlights that dietary antioxidants ( from F & V) induce protective innate immune responses in asthma. However, this study had a limitation of a small sample size.

As paediatricians we have been emphasising in general the need to eat more fruits and vegetables .This study provides evidence for the same especially in children with asthma. This can be an appealing strategy in those children wherein there is a strong family history of asthma and atopy.

It is common to give an “Avoid” list to children with recurrent wheeze but it may be a good idea instead to prescribe a “To Give” list of fruits and vegetables instead. This implementation has benefits of having no side effects, and is likely to be widely accepted and adopted by children and their caregivers.